
Reflections on the Past, Present and Future of USDA's Regulation of Agricultural Biotechnology

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In this presentation, I will include a retrospective, breaking things down into arbitrary timeframes. I am defining the past as from the 1950s through 1992, the present from 1993 to 2013, and the future from today onward (Figure 1).

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- **The Past: 1950s – 1992**
 - Promise and concerns
 - Regulation vs Guidance
 - **The Present: 1993 – 2013**
 - Increased implementation demands
 - Increased public engagement
 - **The Future: 2013 →**
 - Guiding principles
 - Considering diverse viewpoints

Figure 1. Past, present and future.

PAST

Not long ago, DNA was identified as heritable material, and last year—2012—we celebrated the 40th anniversary of the creation of the first recombinant-DNA organism, a bacterium (Figure 2). The scientific community came together in the mid 1970s, and as a group said:

Let's take a break. Let's look at the issue of safety. Let's make sure that this new technology can be used safely.

They called on the National Institutes of Health to develop guidelines for the safe use of recombinant-DNA organisms in contained facilities; the guidelines were promulgated in 1976. The first commercial product from a recombinant organism was human insulin, marketed in 1980. And, in 1983, a recombinant plant was first described in the literature. I remember hearing about this as a beginning plant pathologist, and thinking that it would be a great tool for breeders as it touched upon the bedrock principle of using the best possible genetic basis to obtain resistance to pathogens.

The term “modern biotechnology” typically includes recombinant-DNA organisms (Figure 2). In the United States and other countries, cell-fusion refers to combination of distantly related organisms; however, relatively little work has been done in this area. The note at the foot of Figure 2 is a reminder of the varied terminology that is used. Even the federal agencies use different terms, therefore one system cannot be laid on top of another, nationally or internationally. Internationally, “living modified organism” (LMO) is sometimes used, *e.g.* within the Cartagena Protocol. Everyone is familiar with GMO and “transgenic” is commonly used, whereas GEO seems almost archaic

➤ **Recombinant DNA techniques (recDNA)**

- 1950s, DNA role in heredity
- 1972, first recDNA organisms (bacteria)
- 1976, guidelines from National Institutes of Health (USA)
- 1980, first commercial product (insulin)
- 1983, first recDNA plant

➤ **Cell fusion of distantly related organisms**

Note: Definition of terms is inconsistent:

- recDNA, GMO, GEO, LMO, transgenic

Figure 2. Techniques of modern biology.

In my work for a regulatory agency, not only has my background in science been of utility, but so have my high-school civics classes. The combination has been essential in understanding the legal context within which the system operates. A necessary part of this is technical practicality; regulations must be enforceable. Of course, safety is a fundamental

consideration and public policy has a role. Some countries enact public policy aimed at promoting innovation or at tying their regulatory approach into a national system that assists development of the agricultural or the science and technology sector. And in recent years, international obligations have come into play increasingly.

The Coordinated Framework for Regulation of Biotechnology—proposed in 1984 by the White House Office of Science and Technology Policy and finalized in 1986—spells out the basic federal policy for regulating the development and introduction of products derived from biotechnology (Figure 3). This regulatory policy framework was developed to ensure safety of the public and to ensure the continuing development of the fledgling biotechnology industry without overly burdensome regulation. It applies as much today as it did in 1986: in essence, the employment of these techniques does not, in and of itself, raise safety concerns. Also, federal laws, already enacted, cover any safety issues, and, if further regulation is needed, it should be based on the best available scientific information. Furthermore, applications for deregulation should be dealt with on a case-by-case basis.

- The safety risks of GE organisms are not fundamentally different from safety risks posed by non-GE organisms with similar traits.
- The existing laws provide adequate authority.
- Regulation should be science-based and conducted on a case-by-case basis.

Figure 3. Coordinated Framework (1986):
Federal role in the safe use of biotechnology.

APHIS regulation of GE organisms is pursuant to the Plant Quarantine Act (PQA) of 1912 and the Federal Plant Pest Act (FPPA) of 1957. The original acts, which had nothing to do with genetically engineered organisms, were set up so that the federal government would have the ability to prevent plant pests—insects and pathogenic organisms—from coming into the country and moving interstate. These statutes were rolled together, along with the Noxious Weed Act, into the Plant Protection Act of 2000. After vigorous debate—should the USDA operate under federal regulations or operate under an advisory system akin to the National Institutes of Health Guidelines—it was decided to go with a legally binding system under regulations, put in place in 1987.

Every regulation basically comes down to two parts: the item regulated and the activities of that item, which, under APHIS regulations (7CFR Part 340) is termed a “regulated article,” which has two parts to the trigger (Figure 4). The plant has been modified or produced using recombinant-DNA technology to modify the organism; and there has to be a possibility that the genetically engineered plant has a pest risk associated with it. In other words, if a recombinant DNA technique has been employed to modify an organism,

- “Regulated articles” (7 CFR part 340)
 - If the organism has been altered or produced through genetic engineering, **and**
 - If there is a possibility that the GE organism could be a plant pest, i.e.,
 - Donor, recipient, or vector organism is a plant pest
 - “Plant pest” is defined by statute
- Is my GE organism a regulated article?
 - www.aphis.usda.gov/biotechnology/am_i_reg.shtml

Figure 4. What does APHIS-BRS regulate?

and the donor organism, the recipient organism or the vector agent is a plant pest, then the resulting genetically engineered organism is called a “regulated article.”

Over the years, people contacted us: “I’ve read the regulation and still don’t understand whether I have a regulated article.” A few years back, APHIS set up a website (Figure 4) that gives instructions on how to put together a letter of enquiry regarding a proposed or actual organism. No risk assessment involved. The feedback from APHIS is in terms of, “Yes, that meets the definition of a regulated article,” or “No, it does not meet the definition of a regulated article.” Fourteen such letters and APHIS’s responses are posted on the website. This has been an eye-opener for some who thought that if genetic engineering techniques are involved, the item automatically falls under the regulations, which is not the case.

Figure 5 shows the activities that require authorization: importation to the United States; movement from state to state (not intrastate movement); and/or release into the environment. One of two authorization mechanisms may be applicable: the original permitting procedure that has been part of the regulation since 1987; the notification procedure which was introduced in 1993 to provide a more streamlined approach. Both procedures set out how the regulated article is to be authorized for importation, interstate movement and release into the environment.

PRESENT

Twenty years, 1993–2013, is a generous time span for “the present” (Figure 1). In 1993, we added something that the original regulations had no provision for: the commercialization of genetically engineered plants. A farmer could not be expected to obtain permits and notifications every time (s)he moved genetically engineered seed or planted

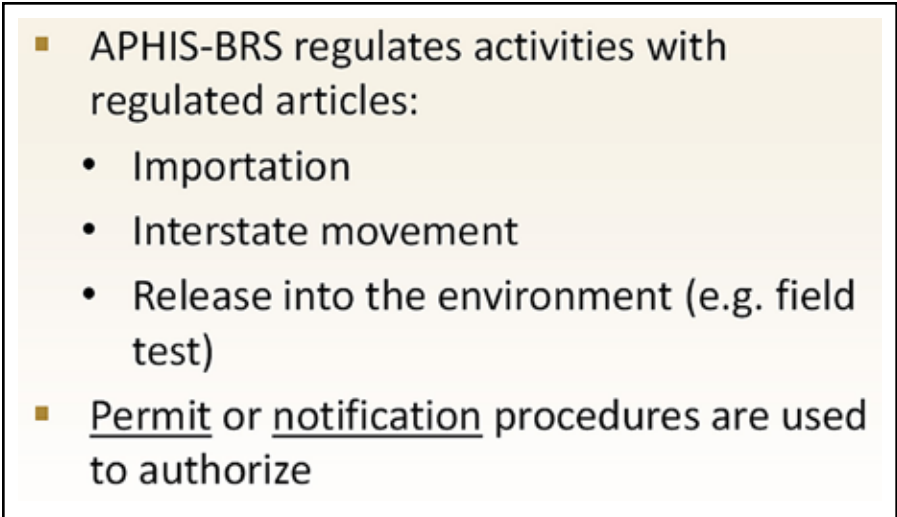
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- APHIS-BRS regulates activities with regulated articles:
 - Importation
 - Interstate movement
 - Release into the environment (e.g. field test)
 - Permit or notification procedures are used to authorize

Figure 5. Introduction of regulated articles.

a genetically engineered crop. We established a procedure whereby someone can petition us, in writing, for review to request that their genetically engineered organism should no longer be a regulated article because it doesn't pose any plant-pest risk. Also, the US public was given the opportunity to be involved in these reviews, which is unusual. The dossier of information submitted to the agency supporting the contention that the genetically engineered organism is not a plant pest is available for public review—and comment—before final APHIS determination.

These petitions involve two evaluations by APHIS. We make a risk assessment—as a stipulation of the Plant Protection Act—to answer the question: *Does the genetically engineered organism pose a plant-pest risk?* And we make an environmental assessment—as a stipulation of the National Environmental Policy Act (NEPA, signed by Richard Nixon in 1970, setting standards for federal agencies to appraise the significance of environmental impacts that might arise from their decisions¹). Under NEPA, the public again has the opportunity to provide input. This does not determine the agency's decision, but it does inform the decision-making process.

To date, APHIS-BRS has made determinations of non-regulated status in response to over 90 petitions, comprising 16 plant species (Figure 6). Once non-regulated status is granted, the petitioner's obligation under the regulation is finished: there is no license; there is no permit; nothing needs to be reviewed. Progeny derived from the organism through traditional plant breeding also has non-regulated status. For example, hundreds of varieties have been developed from the first glyphosate-tolerant soybean ("HT" in Figure 6) to receive non-regulated status from us in the 1990s. Likewise, hundreds of varieties

¹Back then, the decisions had nothing to do with genetically engineered organisms; they applied to federal agencies responsible for building bridges, dams, roads, *etc.*

that have been developed from the early *Bt* corn genotypes (“IR” in Figure 6), with no obligation to apply for deregulation. Our statute is unrelated to commercialization; it strictly deals with safety issues. Some genetically engineered plants under regulation are actually being used as sources for commercial purposes, but all are being grown under permits.

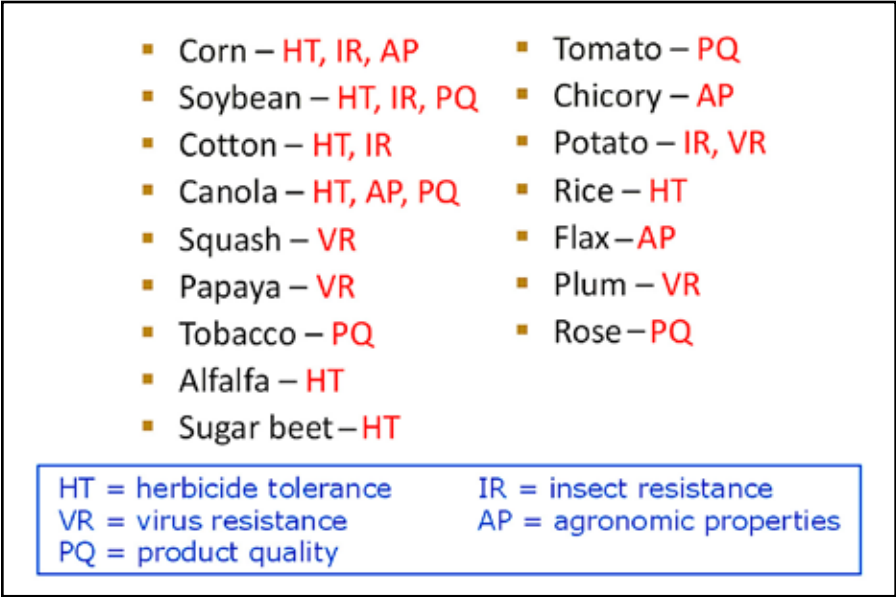


Figure 6. Genetically engineered species with non-regulated status under 7CFT part 340.

Commercialization is not under APHIS’s authority. Whether a product is commercialized is market-driven. The left column in Figure 6 shows products that are on the market as of June 2013, including the high-profile cases of herbicide-tolerant alfalfa and sugar beet, and less well known tobacco with reduced nicotine. Dennis Gonsalves’s² papaya is also in the left column, And we have everything from insect resistance (“IR”) and drought tolerance (“AP”) in corn, through herbicide tolerance in canola (“HT”) to high oleic acid content in soybean (“PQ”). The right column includes the FlavrSavr[®] tomato and another slow-ripening high-solids tomato. Male-sterile chicory (“AP”), sometimes called radicchio—developed in Belgium in the mid-1990s—has non-regulated status, but does not have consumer approval in Europe. Several herbicide-tolerant rice lines have been through the system, but commercialization is pending, subject to approvals in other countries. The blue rose (“PQ”) and Ralph Scorza’s plum³ (“VR”) are also in the column on the right; they are gearing up for commercial release of the virus-resistant plum. Some others are on track for commercialization .

²Pages 37–46.

³Page 136.

Recent APHIS-BRS Initiatives

In 2007, we initiated a voluntary compliance-assistance program, with early input from large companies, medium-size companies and public research institutions. An extensive effort in recent years has examined the petition process to make it more efficient. Over the years, we went from a six-month timeframe for completing reviews, to where it was taking up to several years. Petition-process improvement was put into place in 2011. And in 2008 we proposed amending the regulation. In the United States, a regulation is proposed and followed by a public-comment period, after which the regulation may be finalized. In this case, after announcement of the initial proposal, 66,000 comments were received and are still being appraised.

- Scientific integrity
- Public participation
- Communication
- Flexibility
- Risk assessment and risk management
- Coordination
- International cooperation
- Benefits of regulation should justify costs
- Promote innovation while advancing protection goals (health, environment, safety)
- If no significant issues identified, consider not regulating
- Develop performance based regulatory approaches that are predictable and flexible in the face of fresh evidence

Figure 7. Guiding principles for regulating new technologies.

FUTURE

In 2011, a memorandum was issued by the White House Office of Science and Technology Policy in conjunction with the Office of Management and Budget and the US Trade Representative's Office—frequently referred to as the Holdren memo—titled *Principles for Regulation and Oversight of Emerging Technologies*. Although it is not aimed at biotechnology alone, it is similar in tone and emphasis to the *Coordinated Framework for Regulation of Biotechnology*, *i.e.* favoring innovation, having enough regulation as necessary and to also consider that there may be no need for regulation.

Figure 7 shows key principles espoused in the Holdren memo. International cooperation is becoming increasingly important, especially in the biotechnology area. Again, the benefits of a regulation should justify the costs it incurs. Are regulations the best approach? How much leeway is in the system? Technically, if you set up a class of things that are regulated, can you distinguish them from counterparts that are not regulated? Safety, of course, comes into play as part of public policy. The Holdren memo is an example of public policy that sets out international obligations.

The Sanitary and Phytosanitary Agreement under the WTO, which came into being in 1995 says, in essence: “In the absence of good scientific evidence that demonstrates harm to plants, animals or to humans, we should not restrict trade.” This lens may be applied to the regulatory systems in the United States and elsewhere.

The Secretary of Agriculture's Advisory Committee on Biotechnology and Agriculture has, over the past two years, taken up the issue of coexistence. Although this has to do with crops after they're out from under our regulatory system, APHIS-BRS has been involved in helping to bring stakeholders together for on-going discussions.

Figure 8 provides our website and means to obtain stakeholder-information updates via email.

- **USDA-APHIS-BRS on the web:**

- http://www.aphis.usda.gov/biotechnology/brs_main.shtml

- **Become a BRS Stakeholder:**

- Sign up for automatic news and information:

- <http://www.aphis.usda.gov/biotechnology/index.shtml>

- Click on the red envelope at the bottom right corner of the page



Figure 8. For more information.

DAVID HERON is assistant director of Policy Coordination Programs of Biotechnology Regulatory Services, the unit responsible for implementing the biotechnology regulations of the US Department of Agriculture's Animal and Plant Health Inspection Service (APHIS). His primary responsibilities include the development of coherent and coordinated national and international policies, risk assessment, regulatory analysis, communication, and domestic and international regulatory capacity building in agricultural biotechnology.

Dr. Heron has served in the APHIS biotechnology regulatory program since 1991, with the exception of a year during which he served as task manager with the United Nations Environment Programme for eight country projects on the implementation of national biosafety frameworks (Bulgaria, Cameroon, China, Cuba, Kenya, Poland, Namibia and Uganda). He received his BA in biology from Gettysburg College and his PhD in plant pathology from the University of Missouri-Columbia.